Appl. No. 10/598,149 Amdt. dated September 28, 2007 Reply to Office Action of August 28, 2007

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- (original) A truncated thrombomodulin protein derivative comprising EGF (4-6) like domains, a substitution of Leucine for methionine at position 388, and a GGM amino acid motif appended at a carboxy terminus of said derivative.
- (original) The truncated thrombomodulin protein of claim 1 wherein said GGM protein motif is expressed as a protein motif with a non-natural amino acid corresponding to the M amino acid residue.
- (previously presented) A truncated thrombomodulin protein comprising SEQ ID NO:3.
- 4. (original) A truncated thrombomodulin derivative conjugate comprising a truncated thrombomodulin derivative and a polymer; wherein the thrombomodulin derivative comprises EGF (4-6) like domains, a substitution of Leucine for methionine at position 388, and a GGM amino acid motif appended at a carboxy terminus of said derivative.
- (original) The conjugate of claim 4 wherein the polymer comprises polyethylene glycol.
- 6. (original) A truncated thrombomodulin nucleic acid derivative comprising EGF (4-6) like domains, a substitution of Leucine for methionine at position 388, and a nucleic acid sequence capable of encoding a Gly Gly Met motif appended at a carboxy terminus of said derivative.
- (previously presented) The thrombomodulin nucleic acid derivative of claim 6 comprising SEQ ID NO:1.

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- 8. (original) A method of generating a purified truncated thrombomodulin derivative protein, wherein the protein comprises EGF (4-6) like domains, a substitution of Leucine for methionine at position 388, and a non-natural amino acid; comprising the steps of providing a truncated thrombomodulin nucleic acid sequence; recombinantly expressing said nucleic acid sequence in the presence of a non-natural amino acid precursor; and purifying a recombinant expression product; thereby generating a purified truncated thrombomodulin derivative protein.
- (original) The method of claim 8 wherein said nucleic acid sequence is SEQ ID
 NO:1
- 10. (original) The method of claim 8 wherein the non-natural amino acid is selected from the group consisting of: methionine analogues, alanine analogues, phenylalanine analogues, leucine analogues, proline analogues and isoleucine analogues.
- (original) The method of claim 10 wherein said methionine analog is L-2-amino-4azido-butanoic acid.
- (original) The method of claim 8 wherein the non-natural amino acid is located at a C-terminal portion of the construct.
- 13. (original) A method of site-specific PEGylation of a bioactive protein, comprising identifying an amino acid residue capable of alteration wherein the alteration does not substantially impair a protein activity; altering said amino acid residue; integrating a non-natural amino acid residue into said bioactive protein at a site, and conjugating a PEG polymer to said non-natural amino acid at the site.
- (original) The method of claim 13 wherein the bioactive protein is thrombomodulin.

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- (original) The method of claim 13 wherein the bioactive protein is a thrombomodulin derivative.
- (original) A conjugate of a thrombomodulin protein or a thrombomodulin derivative and a polymer.
- 17. (original) The conjugate of claim 16 wherein the polymer is PEG.
- 18. (original) The conjugate of claim 16 wherein the polymer can confer a property for the conjugate selected from the group consisting of: an increase in plasma half-life, stability against proteolytic cleavage, and a decrease of protein immunogenicity, or combination thereof.
- 19. (original) The conjugate of claim 16 wherein the conjugate is soluble.
- (original) A thrombomodulin derivative comprising a catalytically active site capable of activating protein C and a non-natural amino acid.
- (original) The thrombomodulin derivative of claim 20 wherein the derivative comprises an extracellular portion of thrombomodulin.
- (original) The thrombomodulin derivative of claim 20 wherein said active site comprises EGF (4-6) domains.
- (original) The thrombomodulin derivative of claim 20 conjugated via said nonnatural amino acid to a linear or branched natural or synthetic polymer.
- 24. (original) The derivative of claim 23 wherein said linear or branched synthetic polymer is selected from the group consisting of poly(t-butyl acrylate), poly(t-butyl methacrylate), polyacrylamide, glycolipid and their mimetics; and other polymers; glycoproteins and their mimetics, poly(arginine), polysaccharides and their mimetics; and other polymers as would be understood in the art.

Claims 25-60 (canceled)